REMARKS

Upon entry of this amendment, claims 1-7, 9, 11-16 and 19 are pending in the instant application. Claims 10, 17-18 and 21-22 have been cancelled, and Applicants reserve the right to prosecute that subject matter, as well as the originally presented claims, in continuing applications. Claims 1, 4, 5, 11 and 19 have been amended herein. Support for the claim amendments presented herein is found throughout the specification and in the claims as originally filed. For example, support for the amendment to claims 1, 4 and 5 is found at least at page 14, lines 15-19. Claim 11 has been rewritten as an independent claim, and support for this amendment is found at least at page 22, lines 20-23; at page 33, lines 11-19; in Figures 1 and 8; and in claims 1 and 10 as originally filed. Support for the amendment to claim 19 is found at least at page 14, lines 20-21 and in claim 15 as originally filed. Accordingly, no new matter has been added by these amendments.

I. Election

The Examiner has indicated that newly submitted claims 21 and 22, and claims 17-18 as amended in the previous Response and Amendment, mailed December 17, 2003, read on a non-elected invention. According to the Examiner, these claims read on a method of screening for a "generic bridging domain", while the invention originally examined is drawn to constructs that contain a generic bridging domain.

To expedite prosecution of the instant application, claims 17-18 and 21-22 have been cancelled herein without prejudice or disclaimer. Thus, any objections to these claims have been rendered moot and should be withdrawn.

II. Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 4 and 5 have been rejected as being indefinite and ambiguous. According to the Examiner, claim 1 recites "a tripartite construct having three functional domains", which indicates "the presence of three parts of a physical construct or a construct of or divided into three parts." The Examiner has stated that it is not clear how completely overlapping domains would be part of a tripartite construct comprising three functional domains.

Applicants note that claim 1 has been amended herein to recite purified functional polynucleotides that contain three functional domains – an actuator domain, a receptor domain, and a bridging domain that includes a communication module. Thus, amended claim 1 does not require a "three part" physical construct. Moreover, all references to a "tripartite construct" have been removed from the pending claims, as amended.

As acknowledged by the Examiner and disclosed in the instant specification at page 14, lines 15-19, the term "domain" is a functional designation, not a physical one. Thus, the claimed polynucleotides contain three functional domains (actuator, receptor and bridging), but the nucleotide sequence(s) of these domains can be overlapping (*i.e.*, partially or wholly) or non-overlapping, as recited by amended claims 4 and 5. Accordingly, Applicants submit that claims 4 and 5, as amended, are clear and unambiguous, and this rejection should be withdrawn.

III. Claim Rejections Under 37 C.F.R. § 1.75(c)

Claims 10 and 19 have been rejected as being in improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 10 has been cancelled herein without prejudice or disclaimer. Thus, any rejection of this claim has been obviated and should be withdrawn.

In addition, claim 19 has been amended to recite that the polynucleotide prepared using the method of claim 15 is RNA. Thus, amended claim 19 is limited to a process of preparing RNA polynucleotides, whereas its parent claim, claim 15, is directed to a process for preparing polynucleotides. As described throughout the specification, *e.g.*, at page 14, lines 20-21, the polynucleotides of the claimed invention are RNA, RNA analogues, DNA, DNA analogues and mixtures thereof. Thus, the scope of claim 15 is greater than the scope of its dependent claim, claim 19. As such, Applicants submit that claim 19 is in proper dependent form in compliance with 37 C.F.R. § 1.75(c), and this rejection should be withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 102

The Examiner has maintained the rejection of claims 1-7, 9-16 and 19 under 35 U.S.C. §102(a) as being anticipated by Araki *et al.*, *Nucleic Acids Research*, vol. 26(14): pp. 3379-3384 (1998) ("Araki"). The rejection of claims 1-4, 6, 7, 9-15 and 19 under 35 U.S.C. § 102(b) as

being anticipated by Tang *et al.*, *Chemistry and Biology*, vol. 4(6): pp. 453-59 (1997) ("Tang") has also been maintained.

According to the Examiner, Araki and Tang describe allosteric hammerhead ribozymes that contain an actuator domain, a receptor domain and a communication module that is a "generic" reporter of an occupation state of the receptor domain. The Examiner has also indicated that Applicants' arguments filed in the 12/17/03 Response and Amendment are not persuasive. In particular, the Examiner has stated that the specification does not offer a specific definition of the term "generic bridging domain", and that the claims do not require that the "linking regions be capable of functioning in context with any aptamer." (Office Action, page 7).

Claims 1 and 15 (and their respective dependent claims) are directed to polynucleotides that include a functional bridging domain having a communication module that acts as a generic reporter of the occupation status of the receptor domain (*i.e.*, whether the signaling agent is present (*e.g.*, bound) or absent (*e.g.*, unbound)), as well as methods of producing for such polynucleotides.

Applicants submit that the term "generic reporter" is defined throughout the specification, particularly in Example 3, paragraph 1. For example, the specification teaches that the bridging domains serve as generic reporters indicating "the occupation state of different appended aptamers [(*i.e.*, receptor domains)] regardless of the particular ligand specificities" (*See e.g.*, specification at page 33, lines 11-19). In addition, the specification provides examples in which the generic reporter bridging domains are used in conjunction with several "different appended aptamers" of varying ligand specificities, including, for example, the FMN aptamer shown in Figure 4A, the theophylline aptamer shown in Figure 6A, and the cNMP-regulated aptamers shown in Figures 10A and 10G. Thus, the "generic reporter" is defined and exemplified as a linking domain that retains the ability to function as a communication module when appended to a variety of different aptamers.

The term "generic reporter", as recited by the pending claims, should be given "the broadest reasonable interpretation consistent with the specification." (*See* MPEP 2111). Therefore, Applicants submit that the generic reporters of the claimed invention are linking regions that function as a communication module when used in conjunction with several aptamers having varying ligand specificities.

Araki and Tang, however, fail to describe or suggest multidomain polynucleotides having a generic reporter that is functional when appended to several different receptor domains.

Araki

The Araki reference describes linking regions that function when appended to one specific receptor domain, the FMN aptamer (*See* Araki, p. 3380, col. 2, "Results and Discussion," first paragraph, and Figure 1). There is no teaching or suggestion in the Araki reference that the bridging domains shown in Figure 1 can be used with *any* aptamer other than the FMN aptamer, let alone that the Araki linking regions would retain the same, or possess better, function (*i.e.*, the ability to modulate the activity of the hammerhead ribozyme domain), when coupled to several aptamer domains. Araki, therefore, fails to disclose or suggest the generic reporter capable of functioning in context with any aptamer, as used in the claimed polynucleotides and methods. Accordingly, claims 1-7, 9-16 and 19 are novel over the Araki reference, and Applicants request that the Examiner withdraw this rejection.

Tang

The Tang ribozyme constructs contain an actuator domain (catalytic), a receptor domain (ATP and theophylline aptamer domain), and a linking region. Tang describes seven ATP dependent ribozyme constructs, H1-H7 (shown in Table 1), with variable stem II portions, and the H8 ribozyme construct, which contains the same stem II portion as the H3 construct linked to a theophylline aptamer domain (*i.e.*, receptor domain), instead of the ATP aptamer domain (*i.e.*, receptor domain) of H3. The Examiner notes that both the theophylline dependent (H8) and ATP dependent (H3) ribozyme constructs contain the same stem II portion and therefore stem II functions in a generic manner.

However, there is no teaching or suggestion in the Tang reference that the shared stem II region of the H3 and H8 constructs would retain the same, or possess better, function (*i.e.*, the ability to modulate the activity of the hammerhead ribozyme domain), when coupled to other aptamer domains. Tang does not indicate that the stem II portion in ribozyme constructs H1-H7 will function as a generic reporter with any aptamer domain, nor does Tang disclose that the aptamer domains are interchangeable for any other aptamer domain. In fact, the stem II portions in constructs H1-H7 are variable, and thus stem II cannot be considered a generic reporter.

Specifically, Tang discloses that construct H3 is based on H1 with a modified stem II to carry the ATP aptamer, and exhibits ATP dependent inhibition of ribozyme function. Construct H5 contains an expanded Stem II, from 4 to 7 base pairs, and this modification in Stem II eliminates ATP dependent inhibition of ribozyme function. Constructs H6 and H7 contain a modified stem II from H5, where the Waston-Crick based pairs in stem II are replaced with less stable G-U mismatches to weaken stem II, and these constructs display ATP dependent allosteric induction instead of inhibition.

Tang does not disclose that constructs H1-H2, or H4-H7 retain an allosteric effect on ribozyme function regardless of whether an ATP or theophylline aptamer, or any other aptamer is attached. Tang discloses that only one construct, H8, (which is analogous to H3), can function with either an ATP or a theophylline aptamer. Thus, constructs H8 and H3 contain the same stem II portion which differs from H1-H2 and H4-H7. The fact that this stem II region is functional with 2 different aptamers is not sufficient to indicate it is functional with any aptamer domain regardless of ligand specificity such as the present invention discloses. Tang, therefore, fails to disclose or suggest a generic reporter used in the claimed polynucleotides and methods. Accordingly, claims 1-7, 9-16 and 19 are novel over this reference, and this rejection should be withdrawn.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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